The Reactivities of Non-heme Iron(III)peroxo and Iron(IV)oxo Complexes are Tuned by Presence of a Cis Carboxylato, Alkoxido or Pyridine Donor
**Introduction**

Slight changes in the coordination sphere of an iron centre in the active site of enzymes lead to significant changes in their reactivity exemplified by iron non-heme enzymes in the switch from reversible binding of dioxygen in hemerythrin to activation of dioxygen in the related enzyme methane monoxygenase (Scheme 9.1). The donor ability of the first coordination sphere donor dictates the splitting of the ligand field of the metal ion(s), hence determining properties such as the electronic structure, spin state and reduction potential giving the enzymes their individual function. The active site of hemerythrin is rich in histidines, whereas methane monoxygenase has an active site rich in carboxylate donors. The oxygen-rich environment makes the basis of an enzyme, which can fully split the double bond of dioxygen, subsequently exposing a reactive iron(IV) intermediate useful for hydroxylation of the strong C-H bond of methane.

![Scheme 9.1](image)

**Scheme 9.1.** Illustration of the structurally related active sites of the non-heme iron enzymes hemerythrin and methane monoxygenase.

In the field of non-heme iron complexes the significance of varying the supporting ligand has also been widely explored. Several groups have for instance shown that methylation of the ligand can convert iron(III)peroxo species from low-spin to high-spin species, and comparison of the catalytic capabilities of $\text{[Fe}^{\text{II}}(\text{TPA})(\text{MeCN})]^2+$ and $\text{[Fe}^{\text{III}}(6-\text{Me}_3\text{TPA})(\text{MeCN})]^2+$ in substrate oxidation of cyclooctene with $\text{H}_2\text{O}_2$ shows that the methylation of the ligand increases the product distribution of epoxide to diol from 1:1.2 to 1:7. Further evaluation of a series of $\text{[Fe}^{\text{IV}}\text{O(TPA)(X)}]^2+/+$ complexes ($X = \text{MeCN}, \text{OTF}^-, \text{Cl}^-, \text{Br}^-$) has shown that substitution of the cis donor $X$ does not influence the characteristic features of the iron(IV)oxo complexes such as the Fe-O distance, Mössbauer parameters and the energy of the XAS pre-edge. However, the coordination of $X$ is evident by differences in the absorption bands in the near-IR region (720-800 nm). On the other hand substituting the donor $X$ trans to the Fe$^{\text{IV}}=$O moiety in $\text{[Fe}^{\text{IV}}\text{O(TMC)(X)}]^2+$ ($X = \text{MeCN}, \text{HO}^-, \text{N}_3^-, \text{CN}^-, \text{OCN}^-, \text{SCN}^-, \text{OTF}^-$) was demonstrated to cause changes in NIR absorption spectra, the X-ray absorption pre-edge intensities, the quadrupole splitting parameters and the $\nu_{\text{Fe}=\text{O}}$ frequencies. Investigation of the performance of $\text{[Fe}^{\text{IV}}\text{O(TMCS)(X)}]^2+$ ($X = \text{MeCN}, \text{OTf}^-$) and the related complex $\text{[Fe}^{\text{IV}}\text{O(TMCS)}]^2+$ (with an anchored axial thiolate)
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in hydrogen atom transfer (HAT) from O-H and C-H bonds in phenol and alkylaromatic molecules, respectively, revealed that there is a correlation between the HAT reactivity and the reduction potentials of the iron(IV)oxo species. This trend reflects the donor ability of the *trans* donor. The most reactive species was the iron(IV)oxo complex, $[\text{Fe}^{IV}\text{O}(\text{TMCS})]^{2+}$, showing the lowest Fe$^{III}$/Fe$^{IV}$ reduction potential.

Non-heme iron(III)-hydroperoxo species based on an ethylenediamine backboned ligand, $[\text{Fe}^{III}(\text{OOH})(\text{Rtpen})]^{2+}$, were first reported in the 90’s and have extensively been studied, where the R-group primarily is either a non-coordinating donor (N5) or a nitrogen donor (N6) (Scheme 9.2, Rtpen = N-R-N,N’,N’-tris(2-pyridylmethyl)ethane-1,2-diamine). In contrast to these first reports on ethylenediamine backboned iron(III)-hydroperoxides with only nitrogen donors, we have reported that the introduction of a carboxylate in the coordination sphere causes distinct behaviour in $\text{H}_2\text{O}_2$ activation for N4O and N5O based iron complexes. In the case of $[\text{Fe}(\text{OOH})(\text{Htpena})]^{2+}$ disproportionation of $\text{H}_2\text{O}_2$ was observed. Upon homolytic O-O bond cleavage, a highly reactive iron(IV)oxo species, $[\text{Fe}^{IV}\text{O}(\text{Htpena})]^{2+}$, is generated. The change in reactivity pattern is ascribed to an increased oxyl radical character of the iron(IV)oxo species compared to the N5 and N6-based systems. Simultaneously with the generation of $[\text{Fe}^{IV}\text{O}(\text{Htpena})]^{2+}$, hydroxyl radicals are formed, and in the absence of an excess of $\text{H}_2\text{O}_2$ or an external substrate, decomposition of the catalyst will consequently take place. In the light of these recent results we now compare the reactivity of the $[\text{Fe}(\text{tpena})]^{2+}$ and $[\text{Fe}(\text{tpen})]^{2+}$ towards the oxidation of cyclohexanol by $\text{H}_2\text{O}_2$. Moreover, the ethylenediamine backboned iron(III)-hydroperoxo complex, $[\text{Fe}(\text{OOH})(\text{HtpenO})]^{2+}$ (Scheme 9.2) is spectroscopically characterized and included in the reactivity studies in order to evaluate how changing a coordinating donor ligand from a pyridine to a carboxylate or an alkoxide moiety affects the reactivity of the catalysts in the activation of $\text{H}_2\text{O}_2$. The carboxylate unit plays an important role for the activity of e.g. $\text{O}_2$-dependent enzymes. Similarly, the hydroxylated amino acid residues serine and threonine play crucial roles in the activity of various enzyme classes such as proteases and kinases. [20,21]

**Scheme 9.2.** The general chemical structure of the ethylenediamine backboned ligands, and the R-groups of the ligands examined in this study: tpen = $N$-$N,N',N'$-tetrais(2-pyridylmethyl)ethylenediamine], tpenOH = $N$-$N,N',N'$-tris(2-pyridylmethyl)ethylenediamine-$N'$-ethanol and tpena = $N$-$N,N',N'$-tris(2-pyridylmethyl)ethylenediamine-$N'$-acetate. Abbreviations Htpena and HtpenO indicate that one of the pyridyl units is protonated rather than the alcohol group or the carboxylic acid, respectively.
Results and Discussion

Oxidative Properties and Solution State Chemistry of [Fe(tpenO)]^{2+}

When the solid state precursor [FeCl(tpenOH)][PF_6] is dissolved in methanol or acetonitrile, yellow solutions with a maximum absorbance band at either 393 nm (ε = 2000 M^{-1} cm^{-1}) or 398 nm (2100 M^{-1} cm^{-1}) respectively, are generated. The cyclic voltammogram (Figure 9.1a, blue) of [FeCl(tpenOH)][PF_6] in acetonitrile displays a reversible redox Fe^{II}/Fe^{III} wave at 0.17 V vs. Fc/Fc^+, which is located between the reversible Fe^{II}/Fe^{III} redox waves observed for [Fe(tpen)]^{2+} (0.39 V) and [Fe(tpena)]^{2+} (0.04 V). Reports on derivatives of [Fe(tpen)]^{2+} (all N6) demonstrate how the reversible Fe^{II}/Fe^{III} redox potentials are only slightly shifted (< 70 mV difference), when the first coordination sphere is conserved. The remarkable span of 350 mV in Fe^{II}/Fe^{III} reduction potentials among [Fe(tpen)]^{2+}, [Fe(tpenO)]^{2+} and [Fe(tpena)]^{2+} therefore demonstrates the consequence of replacement of one donor in the first coordination sphere from a pyridine to an alkoxide or a carboxylate.

**Figure 9.1.** (a) CV of acetonitrile solutions of [Fe(tpena)]^{2+} (green), [Fe(tpenO)]^{2+} (blue) and [Fe(tpen)]^{2+} (black). [Fe] = 0.5 mM. Scan rate 100 mV s^{-1}. Electrolyte solution: 0.1 M TBAClO_4 in acetonitrile (b) Solution state EPR (black) of [FeCl(tpenOH)][PF_6] dissolved in MeOH and flash-freezed after 10 min. Two rhombic low-spin iron(III) signals are simulated in red and blue. Sum of the fitted spectra is shown in grey. (c) ESI-MS spectrum of [FeCl(tpenOH)][PF_6] (MeCN, pos. mode). Assignment of ions: m/z 216.575 [Fe^{II}(tpenOH)]^{2+} (C_23H_28FeN_5O calcd. 216.578), 432.146 [Fe^{II}(tpenO)]^{2+} (C_23H_28FeN_5O calcd. 432.148) and 468.118 [Fe^{II}(tpenOH)Cl]^{2+} (C_25H_27ClFeN_5O calcd. 468.125) (d) Structures of fac-[Fe(tpenO)]^{2+} and mer-[Fe(tpenO)]^{2+}. 
The Reactivities of Non-Heme Iron(III)peroxo and Iron(IV)oxo Complexes are Tuned by Presence of a Cis Carboxylate, Alkoxido or Pyridine Donor

The lower Fe$^{II}$/Fe$^{III}$ redox potential of [Fe(tpenO)]$^{2+}$ compared to [Fe(tpen)]$^{2+}$ indicates an easier accessibility to higher oxidation states. Solution state EPR spectra of [FeCl(tpenOH)][PF$_6$] dissolved in MeOH show that samples, which are flash-freezed immediately after dissolution, exhibit no EPR signal. However, if the EPR sample is not flash-freezed till after 10 minutes upon dissolution, two rhombic low-spin iron(III) signal are observed ($S = \frac{1}{2}, g = 2.33, 2.15, 1.93$ and $g = 2.40, 2.17, 2.00$, Figure 9.1b). The detection of EPR-active species demonstrate that the solid state iron(II) precursor [FeCl(tpenOH)][PF$_6$] is oxidized in solution over time. Despite the lower redox potential, it is possible to isolate iron(II)-tpenOH based complexes, whereas it has to date only been possible to isolate iron(III)-tpena based complexes even when starting from iron(II) salts.$^{[18,26]}$ Oxidation to iron(III) will increase the oxophilicity of the iron suggesting that [Fe$^{III}$(tpenO)]$^{2+}$ is the major species found in solution, hence tpenO can use its full potential as a hexadentate ligand with one alkoxide donor and three pyridines around an iron centre. The ESI-MS spectrum of [FeCl(tpenOH)][PF$_6$] (Figure 9.1c) consistently shows a base peak of m/z 432.146 which can be assigned to [Fe$^{II}$(tpenO)]$^{+}$. Two diastereoisomers of [Fe(tpena)]$^{2+}$ have been spectroscopically characterized.$^{[17]}$ The two low-spin iron(III) signals observed in Figure 9.1b indicate that two diastereoisomers are also present for [Fe(tpenO)]$^{2+}$ in solution: $fac$-[Fe(tpenO)]$^{2+}$ and $mer$-[Fe(tpenO)]$^{2+}$ (Figure 9.1d). The three pyridine groups are located in a facial geometry in [FeCl(tpenOH)][PF$_6$], which could suggest that $fac$-[Fe(tpenO)]$^{2+}$ is the most stable, and thus the major species in solution due to a simple substitution of the chloride with the alkoxide.

![Normalized absorption](image)

**Figure 9.2.** Characterization of [Fe(tpen)](PF$_6$) (black), [FeCl(tpenOH)]PF$_6$ (blue) and [Fe$_2$O(Htpena)$_2$](ClO$_4$)$_4$ (green) with (a) solid state IR spectroscopy and (b) solution state IR spectroscopy recorded in d3-MeCN. The spectrum of d3-MeCN is shown in grey.

The crystal structure of [FeCl(tpenOH)][PF$_6$] displays coordination of all three pyridines. The alcohol arm of tpenOH is protonated and non-coordinated.$^{[15]}$ In agreement with this, a vibrational O-H band is observed at 3418 cm$^{-1}$ in the solid state for [FeCl(tpenOH)][PF$_6$] (Figure 9.2a, blue). Comparison of the solid state IR spectra of [Fe(tpen)](PF)$_6$, [FeCl(tpenOH)]PF$_6$ and [Fe$_2$O(Htpena)$_2$](ClO$_4$)$_4$ shows similar features, but intense bands at 1073 cm$^{-1}$ and 1660 cm$^{-1}$ are observed for [Fe$_2$O(Htpena)$_2$](ClO$_4$)$_4$ which are assigned to C-O and C=O stretches, respectively, associated with the carboxylate donor. Likewise, solution state IR spectra (Figure 9.2b) of the three iron complexes show similar features. The solvent, acetonitrile, has strong bands in the region of 600-1700 cm$^{-1}$, hence deuterated acetonitrile was used for practical reasons. In the
solution state IR spectrum of $[\text{Fe}_2\text{O} \text{(Htpena)}_2] \left( \text{ClO}_4 \right)_4$, two intense bands are seen at 1715 cm$^{-1}$ and 1675 cm$^{-1}$. Solution state Mössbauer spectroscopy of a similarly prepared iron tpena solution shows that $[\text{Fe(tpena)}]^{2+}$ and $[\text{Fe}_2\text{O} \text{(tpenaH)}_4]^{4+}$ co-exist in acetonitrile,[28] hence the bands at 1715 cm$^{-1}$ and 1675 cm$^{-1}$ are assigned to C=O stretches related to these two iron species. It was not possible to assign any bands to a C–O stretch for neither $[\text{Fe(tpena)}]^{2+}$, $[\text{Fe}_2\text{O} \text{(tpenaH)}_2]^{4+}$ nor $[\text{Fe}^{III} \text{(tpenO)}]^{2+}$ (deuturated acetonitrile has strong bands from 600 to 1200 cm$^{-1}$).

**Formation of Iron(III) Hydroperoxo and Peroxo Species**

As previously reported the purple iron(III) hydroperoxido species $[\text{Fe(OOH)(Htpeno)}]^{2+}$ ($\lambda_{\text{max}} = 537$ nm) is formed by addition of an excess of $\text{H}_2\text{O}_2$ (2 - 300 eq.) to $[\text{FeCl(tpenOH)}][\text{PF}_6]$ dissolved in MeOH.[15] $[\text{Fe(OOH)(Htpeno)}]^{2+}$ shows significantly shorter half-life compared to the N5/N6 ethylenediamine ligand-based systems (minutes vs. several hours). Originally, the lower stability of $[\text{Fe(OOH)(Htpeno)}]^{2+}$ compared to the N5/N6 systems was rationalized by intermolecular hydrogen-bonding between the decoordinated ethylalcohol arm and the FeOOH moiety. However, examination of solutions of $[\text{Fe(OOH)(Htpeno)}]^{2+}$ with a colorimetric approach (Hantzsche reaction[29]) confirmed the presence of formaldehyde suggesting that methanol oxidation occurs and therefore explaining the lower stability. Quantification of the formaldehyde showed 8 % yield w.r.t. $\text{H}_2\text{O}_2$ concentration (50 eq., 1.5 mM [Fe]) 15 min after the addition of $\text{H}_2\text{O}_2$. The lower stability of $[\text{Fe(OOH)(Htpeno)}]^{2+}$ in methanol compared to $[\text{Fe(OOH)(tpen)}]^{2+}$ suggests structural differences between the two species. $[\text{Fe(OOH)(Htpena)}]^{2+}$ cannot be spectroscopically detected in methanol due to an even more rapid methanol oxidation (formaldehyde yield of 35 % w.r.t. $\text{H}_2\text{O}_2$[18]), hence we suggest that $[\text{Fe(OOH)(Htpeno)}]^{2+}$ is based on a N4O donor sphere with a pendant pyridine arm. Interestingly, the trend in stability of the iron(III)hydroperoxides in methanol reflect the trend in Fe$^{II}$/Fe$^{III}$ redox potential of the precursor iron complex, i.e. $[\text{Fe(OOH)(tpen)}]^{2+}$ has the longest life-time in methanol and $[\text{Fe(tpen)}]^{2+}$ has the highest Fe$^{II}$/Fe$^{III}$ redox potential, whereas $[\text{Fe(OOH)(Htpena)}]^{2+}$ is not observed in methanol due to methanol oxidation and $[\text{Fe(tpena)}]^{2+}$ has the lowest Fe$^{II}$/Fe$^{III}$ redox potential.

![Figure 9.3](image_url)

**Figure 9.3.** (a) Raman spectra of $[\text{Fe(tpenO)}]^{2+}$ (black) with addition of 50 eq. $\text{H}_2\text{O}_2$ to generate $[\text{Fe(OOH)(Htpeno)}]^{2+}$ (red) and with additional 10 eq. Et$_3$N to form $[\text{Fe(OO)(Htpeno)}]^{+}$ (green) (-25 °C, [Fe] = 3 mM, $\lambda_{\text{exc}} = 785$ nm) (b) Solution state EPR of $[\text{Fe(tpenO)}]^{2+}$ in MeOH with addition of 50 eq. $\text{H}_2\text{O}_2$ (black, 100 K, [Fe] = 3 mM, microwave frequency 9.30555 GHz). Individual fitted spectra are seen in red and blue. Sum of the fitted spectra is seen in grey.
Investigation of [Fe(OOH)(HtpenO)]$^{2+}$ with resonance Raman spectroscopy ($\lambda_{\text{exc}}$ 785 nm) showed resonance enhanced bands at 619 cm$^{-1}$ and 800 cm$^{-1}$ (Figure 9.3a) assigned to $v_{\text{Fe-O}}$ and $v_{\text{O-O}}$ vibrations, respectively. The EPR spectrum of a frozen solution showed two rhombic low-spin iron(III) ($S = \frac{1}{2}$) signals with $g = 2.21, 2.14, 1.97$ and $g = 2.25, 2.15, 2.00$ (Figure 9.3b, red and blue, respectively). The spectroscopic parameters are similar to previously reported ethylenediamine backboned iron(III) hydroperoxo species (Table 9.1). The two EPR signals are not coincident with those obtained for [Fe(tpenO)]$^{2+}$. The ratio of the spin density for the two EPR signals are however 9:1 both in the spectrum of [Fe(tpenO)]$^{2+}$ (Figure 9.1b) and [Fe(OOH)(HtpenO)]$^{2+}$ (Figure 9.3b) suggesting that fac- and mer-[Fe(tpenO)]$^{2+}$ are not transformed to the same isomer of [Fe(OOH)(HtpenO)]$^{2+}$, but into two different diastereoisomers.

**Table 9.1.** Spectroscopic properties of ethylenediamine backboned iron(III)-hydroperoxide and -peroxide complexes with the supporting ligands tpen, HtpenO and Htpena.

<table>
<thead>
<tr>
<th>Iron species</th>
<th>UV-Visible</th>
<th>EPR$^a$</th>
<th>S</th>
<th>Reference</th>
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</thead>
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<tr>
<td></td>
<td>$\lambda_{\text{max}}$</td>
<td>$v_{\text{Fe-O}}$</td>
<td>$v_{\text{O-O}}$</td>
<td>$g$-values</td>
</tr>
<tr>
<td><strong>fac-[Fe(tpenO)]$^{2+}$</strong></td>
<td>393</td>
<td>2.33, 2.15, 1.93</td>
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<td>this work</td>
</tr>
<tr>
<td><strong>mer-[Fe(tpenO)]$^{2+}$</strong></td>
<td>393</td>
<td>2.40, 2.17, 2.00</td>
<td>½</td>
<td>this work</td>
</tr>
<tr>
<td>[Fe$^{3+}$(OOH)(Htpena)]$^{2+}$</td>
<td>520</td>
<td>2.21, 2.15, 1.96</td>
<td>½</td>
<td>[18]</td>
</tr>
<tr>
<td>[Fe$^{3+}$(OOH)(tpen)]$^{2+}$</td>
<td>541</td>
<td>2.22, 2.15, 1.97</td>
<td>½</td>
<td>[14]</td>
</tr>
<tr>
<td>[Fe$^{3+}$(OO)(HtpenO)]$^{2+}$</td>
<td>537</td>
<td>2.21, 2.14, 1.97</td>
<td>½</td>
<td>[15]</td>
</tr>
<tr>
<td>[Fe$^{3+}$(OO)(Htpena)]$^{+}$</td>
<td>675</td>
<td>2.25, 2.15, 2.00</td>
<td>½</td>
<td>[18]</td>
</tr>
<tr>
<td>[Fe$^{3+}$(OO)(HtpenO)]$^{+}$</td>
<td>716</td>
<td>8.8, 5.0, 4.3, 4.2, 3.5</td>
<td>5/2</td>
<td>[15]</td>
</tr>
<tr>
<td>[Fe$^{3+}$(OO)(tpen)]$^{+}$</td>
<td>755</td>
<td>8.0, 4.3</td>
<td>5/2</td>
<td>[14]</td>
</tr>
</tbody>
</table>

Data for tpena-based complexes were recorded in MeCN, whereas data for on tpen- and tpenO-based complexes were recorded in MeOH. * For $S = \frac{5}{2}$ $g$$^{\text{eff}}$ are denoted.

Addition of only one eq. H$_2$O$_2$ does not result in the formation of an absorbance band at 537 nm expected for [Fe(OOH)(tpenO)]$^{2+}$. One eq. H$_2$O$_2$ is needed to fully pre-oxidize [Fe$^{3+}$(Cl)(tpenOH)]$^{+}$ to [Fe$^{3+}$(tpenO)]$^{2+}$ in freshly made solutions, whereupon the hydroperoxo species can be generated by addition of another one eq. of H$_2$O$_2$. If an excess of H$_2$O$_2$ is directly added, no lag time is spectroscopically observed by UV/vis absorption spectroscopy. In the case of [Fe(OOH)(tpen)]$^{2+}$, lag time is observed even when an excess of H$_2$O$_2$ is added, demonstrating the easier accessibility to higher oxidation states for [Fe(tpenO)]$^{+}$ than [Fe(tpen)]$^{2+}$ cf. the redox potentials of the complexes. Addition of another portion of H$_2$O$_2$ regenerates the chromophore at 537 nm suggesting that no ligand break-down takes place as is the case of [Fe(OOH)(Htpena)]$^{2+}$. The production of O$_2$ (identifiable by visible bubbles in the solution) generated from H$_2$O$_2$ disproportionation in acetonitrile solutions of [Fe(tpen)]$^{2+}$ is not observed for [Fe(tpenO)]$^{2+}$ under the same conditions ([Fe] = 0.5 mM, 50 eq. H$_2$O$_2$) suggesting a less promiscuous reactivity of the [Fe(OOH)(HtpenO)]$^{2+}$ complex compared to [Fe(OOH)(Htpena)]$^{2+}$.

Addition of Et$_3$N to a solution of [Fe(OOH)(HtpenO)]$^{2+}$ causes a deprotonation of the hydroperoxo ligand and generates the green side-on peroxy species [Fe(OO)(HtpenO)]$^{+}$ ($\lambda_{\text{max}}$ 713 nm). The species can also be directly formed by addition of H$_2$O$_2$ under basic conditions. As for the other ethylenediamine backboned ligand systems, this complex is a high-spin iron(III) species ($S = \frac{5}{2}$, $g$$^{\text{eff}}$ = 8.0, 4.3), and the Fe-O and O-O vibrational bands are observed at 472 cm$^{-1}$ and 818 cm$^{-1}$, respectively ($\lambda_{\text{exc}}$ 785 nm, Figure 9.3a.) Both the end-on hydroperoxo and the side-on
peroxide species supported by HtpenO have longer lifetimes than the corresponding complexes supported by Htpena. At -15 °C the $T_{1/2}$ is 30 min for $[\text{Fe(OO)}(\text{HtpenO})]^+$ (10 eq. Et$_3$N, 50 eq. H$_2$O$_2$). However, besides temperature, the stability of $[\text{Fe(OO)}(\text{HtpenO})]^+$ strongly depends on the number of eq. of base added. When only a few equivalents of Et$_3$N are added (< 10 eq.), the 713 nm species can be regenerated by a second portion of H$_2$O$_2$. When a larger excess of base is added (> 30 eq.), a blue-shift of the absorbance band occurs (Figure 9.4). Visible bubbles are simultaneously formed, and the absorbance band disappears within seconds. $[\text{Fe(OO)}(\text{Htpena})]^+$ ($\lambda_{\text{max}}$ 675 nm) is a very unstable species even at -30 °C. We therefore suggest that in the presence of a large amount of base the methylene group next to the oxygen atom in HtpenO is oxidized to a carbonyl unit transforming HtpenO into Htpena (Scheme 9.3). The coincident spectroscopic parameters for $[\text{Fe(OO)}(\text{Htpena})]^+$ and $[\text{Fe(OO)}(\text{HtpenO})]^+$ (except for the UV/vis spectra) together with the instability of the species have prevented further detection of the conversion. The low stability of the side-on peroxides compared to the end-on hydroperoxides suggests that these species are relatively more reactive.

![Figure 9.4](image-url) Conversion of $[\text{Fe(OO)}(\text{HtpenO})]^+$ to $[\text{Fe(OO)}(\text{Htpena})]^+$ over the course of one minute at -30 °C followed by UV/vis absorption spectroscopy (50 eq. H$_2$O$_2$, 30 eq. Et$_3$N, [Fe] = 1 mM).

![Scheme 9.3](image-url) Proposed mechanism of the regioselective ligand oxidation of HtpenO to Htpena in the complex $[\text{Fe(OO)}(\text{HtpenO})]^+$ to generate $[\text{Fe(OO)}(\text{HtpenO})]^+$.
Tuning the Reactivity in Catalytic C-H Oxidation

The different Fe⁹ ⁄Fe¹⁰ reduction potentials of [Fe(tpen)]⁺, [Fe(tpenO)]²⁺ and [Fe(tpena)]²⁺ as well as the differences in stability of their counterpart iron(III)hydroperoxo species in methanol (aka potency in methanol oxidation) indicate differences in reactivity. The oxidative catalytic performance of the three iron complexes towards oxidation of the C-H bonds of cyclohexane (C-H BDE = 99.5 kcal mol⁻¹) was evaluated using H₂O₂ as the terminal oxidant (Table 9.2). Product analysis was performed with GC chromatography, and cyclohexanol and cyclohexanone were detected as the only products.

Table 9.2. Comparison of product distribution during the oxidation of cyclohexane

<table>
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<th>Procatalyst</th>
<th>Product [mM]</th>
<th>Ratio of ketone: alcohol</th>
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<tbody>
<tr>
<td></td>
<td>Cyclohexanone</td>
<td>Cyclohexanol</td>
</tr>
<tr>
<td>No catalyst</td>
<td>0.0(0)</td>
<td>0.0(0)</td>
</tr>
<tr>
<td>Fe(ClO₄)₂</td>
<td>0.0(0)</td>
<td>0.0(0)</td>
</tr>
<tr>
<td>Fe(ClO₄)₃</td>
<td>0.0(0)</td>
<td>4.0(4)</td>
</tr>
<tr>
<td><a href="PF%E2%82%86">Fe(tpen)</a>₂</td>
<td>3.4(2)</td>
<td>5.3(2)</td>
</tr>
<tr>
<td>[FeCl(tpenOH)]PF₆</td>
<td>3.2(2)</td>
<td>3.9(3)</td>
</tr>
<tr>
<td>[Fe₂O(Htpena)₃][ClO₄]₄</td>
<td>3.1(2)</td>
<td>10.6(3)</td>
</tr>
</tbody>
</table>

Reaction conditions: [Fe] (1 mM), cyclohexane (500 mM) and H₂O₂ (100 mM) in 2 ml MeCN at rt under air. The reported values are representing an average of four runs.

The oxidation of cyclohexane to cyclohexanol can be initiated by an iron(IV)oxo-mediated HAT reaction followed by a radical termination with a hydroxyl radical (Scheme 9.4a). Hydroxyl radicals are generated alongside the iron(IV)oxo species from homolytic O-O bond cleavage of the iron(III)hydroperoxides. The oxidation of cyclohexanol to cyclohexanone is a two electron process, which e.g. can be obtained by two consecutive iron(IV)oxo-mediated HATs (Figure 9.4b). Alternatively, cyclohexanone can be formed in an oxygen-dependent pathway (Scheme 9.4c). The peroxy radical can e.g. derive from HAT from hydrogen peroxide (Scheme 9.4d). In a similar study it has been demonstrated that eliminating O₂ from the catalytic experiments, lowers the yield of the ketone product. The present study was not performed under inert conditions due to the known H₂O₂ disproportionation properties of [Fe(tpena)]²⁺. The disproportionation pathway was however minimized by slow addition of H₂O₂ with a syringe pump and an excess of substrate (Fe:H₂O₂:cyclohexane 1:100:500).

In the presence of a simple iron(III) salt such as Fe(ClO₄)₃, similar yields of cyclohexanol were detected (4.0 mM) compared to when [FeCl(tpenOH)]PF₆ (3.9 mM) and [Fe(tpen)](PF₆)₂ (5.3 mM) were used. The use of [Fe₂O(Htpena)₃][ClO₄]₄ however showed increased formation of the cyclohexanol product indicating an enhanced reactivity in HAT reactions towards the strong C-H bonds in cyclohexane, which either originates from a higher reactivity of the iron(III)hydroperoxo species of Htpena or a higher lability of the O-O bond in [Fe(O-CH)(Htpena)]²⁺ to expose the two potential hydrogen atom abstractors: [Fe⁴VO(Htpena)]²⁺ and the hydroxyl radical. Reports comparing the reactivity of non-heme iron(III)hydroperoxo species and the daughter iron(IV)oxo species towards substrate oxidation, including the structural similar [FeOOH(bztpen)]²⁺ (bztpen: N-benzyl-N,N',N'-tris(2-pyridylmethyl)-1,2-diaminoethane), conclude that the iron(III)hydroperoxides are rather sluggish oxidants and that they cannot compete with their daughter iron(IV)oxo species. Furthermore it has previously been shown that when [Fe⁴VO(Htpena)]²⁺ is electrochemically generated in water (i.e. in the absence of chemical
oxidants), it participates in HAT chemistry. On the basis of these reports and the catalytic results presented here, it seems likely that [Fe\textsuperscript{IV}O(Htpena)]\textsuperscript{2+} (rather than [Fe\textsuperscript{III}OOH(Htpena)]\textsuperscript{2+}) is the active metal-based oxidant, and that the potency of [Fe\textsuperscript{IV}O(Htpena)]\textsuperscript{2+} is higher than that of [Fe\textsuperscript{IV}O(HtpenO)]\textsuperscript{2+} and [Fe\textsuperscript{IV}O(Htpen)]\textsuperscript{3+}. Crucially, [Fe(OOH)(Htpena)]\textsuperscript{2+} must also have a relatively higher lability of the O-O bond relative to the other two iron(III)hydroperoxides, hereby also exposing the active iron(IV)oxo species easier.

![Scheme 9.4](image)

**Scheme 9.4.** (a) Oxidation of cyclohexane to cyclohexanol (b) Iron(IV)oxo-mediated oxidation of cyclohexanol to cyclohexanone. (c) Oxygen-dependent formation of cyclohexanone (d) Generation of HOO•.

Based on the lifetimes of [Fe(OOH)(tpen)]\textsuperscript{2+} and [Fe(OOH)(HtpenO)]\textsuperscript{2+} in methanol and the fact, that the C-H bond in cyclohexane is stronger than that in methanol (C-H BDE = 99.5 kcal mol\(^{-1}\) and 96.0 kcal mol\(^{-1}\))\(^{[30]}\), it is expected that [Fe(tpen)]\textsuperscript{2+} and [Fe(tpenO)]\textsuperscript{2+} show no or little reactivity towards cyclohexane with H\textsubscript{2}O\textsubscript{2}. All three catalysts showed the same yields of ketone-product (3.4 mM, 3.2 mM, 3.1 mM), and no formation of cyclohexanone was detected with iron perchlorate salts, indicating that the catalysts are responsible for the oxidation of cyclohexane to cyclohexanone. The C-H bond in cyclohexanol is relatively weaker ((CH\textsubscript{2})\textsubscript{5}CH\textsubscript{2}OH C-H BDE = 92.8 kcal mol\(^{-1}\))\(^{[30]}\) indicating that all three ligand-based iron(IV)oxo species show reactivity towards C-H bonds with bond dissociation energies equal to or less than 92.8 kcal mol\(^{-1}\).

**Conclusion**

This study on substrate oxidations with H\textsubscript{2}O\textsubscript{2} catalysed by a series of non-heme ethylenediamine backboned iron complexes, [Fe(tpen)]\textsuperscript{2+}, [Fe(tpenO)]\textsuperscript{2+} and [Fe(tpena)]\textsuperscript{2+}, \(\text{Fe}^\text{II}/\text{Fe}^\text{III}\) redox potentials of the catalysts are linked to the lability of the O-O bond of the directly generated iron(III)hydroperoxo species as well as the oxidative power of the catalytic active oxidants: iron(IV)oxo species generated upon homolysis of the O-O bond of the iron(III)hydroperoxides. The Fe\textsuperscript{V}/Fe\textsuperscript{II} redox potentials of [Fe(tpen)]\textsuperscript{2+}, ...
The Reactivities of Non-Heme Iron(III)peroxo and Iron(IV)oxo Complexes are Tuned by Presence of a Cis Carboxylate, Alkoxido or Pyridine Donor

[Fe(tpenO)]^{2+} and [Fe(tpena)]^{2+} span over 350 mV, which is caused by the replacement of a pyridyl in the first coordination sphere of the iron metal, by an alkoxide and a carboxylate donor respectively. Consequently, iron(III) oxidation states are stabilized for [Fe(tpenO)]^{2+} and [Fe(tpena)]^{2+}. With the lowest Fe^{II}/Fe^{III} redox potential, [Fe(tpena)]^{2+} performs best in H_{2}O_{2} activation and can hydroxylate the strong C-H bonds in cyclohexane. The life-times of iron(III)hydroperoxides in methanol follows the trend [Fe(OOH)(Htpena)]^{2+} (not observed) < [Fe(OOH)(HtpenO)]^{2+} (seconds) < [Fe(OOH)(tpen)]^{2+} (hours). [Fe(OOH)(HtpenO)]^{2+} and [Fe(OO)(HtpenO)]^{+} were spectroscopically characterized, and [Fe(OO)(HtpenO)]^{+} was demonstrated to undergo base-dependent regioselective oxidation to [Fe(OO)(Htpena)]^{+}. Our findings demonstrate the importance of stabilizing higher oxidation states in the catalysts (+3 vs. +2) in order to afford increased catalytic activity in H_{2}O_{2} activation.

Experimental Section

The iron precursor complexes [Fe(tpen)][PF_{6}]_{2}, [Fe_{2}O(Htpena)]_{2}[ClO_{4}]_{4} and [FeCl(tpenOH)][PF]_{6} were synthesized as previously described.\[^{15,26,34}\] H_{2}O_{2} (50% in water, v/v) and all other chemicals were commercial available and used without further purification.

Generation of [FeOOH(HtpenO)]^{2+} and [FeOO(HtpenO)]^{+}

[FeCl(tpenOH)][PF]_{6} was dissolved in MeOH and 50 eq. H_{2}O_{2} were added to generate [FeOOH(HtpenO)]^{2+}. A further addition of 10 eq. of Et_{3}N deprotonates the transient species to form [FeOO(HtpenO)]^{+}. The base can also be added prior to H_{2}O_{2}, hereby [FeOO(HtpenO)]^{+} is formed instantly.

Instrumentation and methods

UV/Vis spectra were recorded in 1 cm quartz cuvettes on either an Agilent 8453 spectrophotometer with an UNISOKU CoolSpeK UV USP-203 temperature controller or with an Analytikjena Specord S600 with a Quantum Northwest TC 125 temperature controller. IR spectra were either recorded in the solid state on a Spectrum 65 FT-IR spectrometer (PerkinElmer) or in the solution state on a ChiralIR-2X spectrometer (BioTools). Raman spectra were recorded in 1 cm quartz cuvettes at 785 nm with either a RamanFlex (Perkin Elmer) equipped with an Inphotonics industrial probe or a free space laser (75 mW, Ondax, with a 785 nm laser line clean up filter) and collected in back scattering (180°) mode with a Semrock dichroic beamsplitter and a 25 mm diameter/7.5 cm planoconvex lens to focus the laser on the sample and collect the Raman scattering. The Raman scattering was passed through a long pass filter (Semrock) and focused into a Shamrock300 spectrograph (ANDOR technology) and dispersed onto a iDUS-420-BUEX2 CCD camera. Spectra were calibrated with MeCN/toluene (50:50 v/v). The solutions were cooled with a Quantum Northwest TC 125 temperature controller and the spectra were obtained at -25 °C. Baseline correction was performed for all spectra and normalized to the solvent band at 1038 cm⁻¹. EPR spectra (X-band) were recorded on a Bruker EMX Plus CW spectrometer (mod. amp.: 10 G, attenuation: 10 dB) on frozen solutions at 100 K. eview4wr and esimX were used for simulation.\[^{35}\] Cyclic voltammetry was performed on an Eco Chemie Autolab PGSTAT10 Potentiostat/Galvanostat using a standard 3-electrode setup with a Pt disc as working
electrode, a Pt wire as counter electrode and an Ag/Ag⁺ as reference electrode (0.01M AgNO₃ in 0.1M TBACIO₄ in MeCN; TBA: tert-butyl ammonium). The electrolyte solution was a 0.1 M TBACIO₄ in acetonitrile. The working electrode was cleaned by polishing with 0.05 μm alumina followed by sonication and the solutions were purged with nitrogen prior to measurements. The oxidation potential of Fc/Fc⁺ against Ag/Ag⁺ was measured to be 0.08 V, and all oxidation potentials were converted accordingly. Catalysis procedure: H₂O₂ was slowly added over 20 min with a syringe pump, and the reaction mixture was stirred for additional 10 min before it was quenched with Al₂O₃. Biphenyl was subsequently added as an internal standard. Product analysis was performed on a Hewlett Packard 6890 Series gas chromatograph system with a flame ionization detector. Values reported are an average of four runs.
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Bibliography

Chapter 9


[35] by E. Bill (Max-Planck-Institute for Chemical Energy Conversion in Mülheim); available from the author by mail to eckhard.bill@cec.mpg.de, *2016*.